

Mutations and Expressions of Genes Associated with DNA Repair System in Leukemias
Developed by Continuous Exposure to Gamma-Rays at Low-Dose-Rate
- Effect on Murine Hematopoietic Stem Cell Lineage in Continuously Exposed Mice -

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Abstract

Continuous γ -ray irradiation at low-dose-rates (LDRs) and medium-dose-rates (MDRs) also induce leukemias in mice just as acute irradiation induces them at high-dose-rates. It is important to identify the origin of leukemic stem cells (LSCs), as that may make it possible to clarify the process in which normal cells it transforms are transformed into LSCs by LDR radiation. Previous experiments showed that LSCs in mice induced by LDR or MDR radiation had similarities with common lymphoid progenitors (CLPs), mature B cells and granulocytes. We hypothesize that LDR or MDR radiation affects immature and mature cells in the lymphocytic lineage and causes them to transform into LSCs. In this study, we analyzed hematopoietic cells from male SPF B6C3F1 mice exposed to ^{137}Cs γ -rays from 8 weeks of age at LDR of 1 mGy/day (100, 200 and 300 days; total dose = 0.1, 0.2 and 0.3 Gy) and 20 mGy/day (100, 200, 300 and 400 days; total dose = 2.0, 4.0, 6.0 and 8.0 Gy). Mice were also analyzed at days 100, 200, 300 and 400 after MDR irradiation of 400 mGy/day (20 days; total dose = 8.0 Gy). Hematopoietic cells of mice bearing no tumors were analyzed using FACS. The number of CLPs in mice exposed to 20 mGy/day (at days 300 and 400), and 400 mGy/day (at days 200 and 300) were lower than that of the age-matched non-irradiated mice. Meanwhile, the effects of the LDR or MDR irradiation on B cells and granulocytes were relatively small. Hematopoietic stem cells and multi-potent progenitors showed similar alterations to the CLPs and decreased in number when exposed to LDR or MDR radiation. No significant change was observed in the cell numbers of mice exposed to 1 mGy/day, although hematopoietic stem cells showed a transient increase at day 100. It is likely that LDR and MDR radiation-induced leukemias originate from immature cells of lymphocytic lineage involving CLPs, hematopoietic stem cells and multi-potent progenitors.

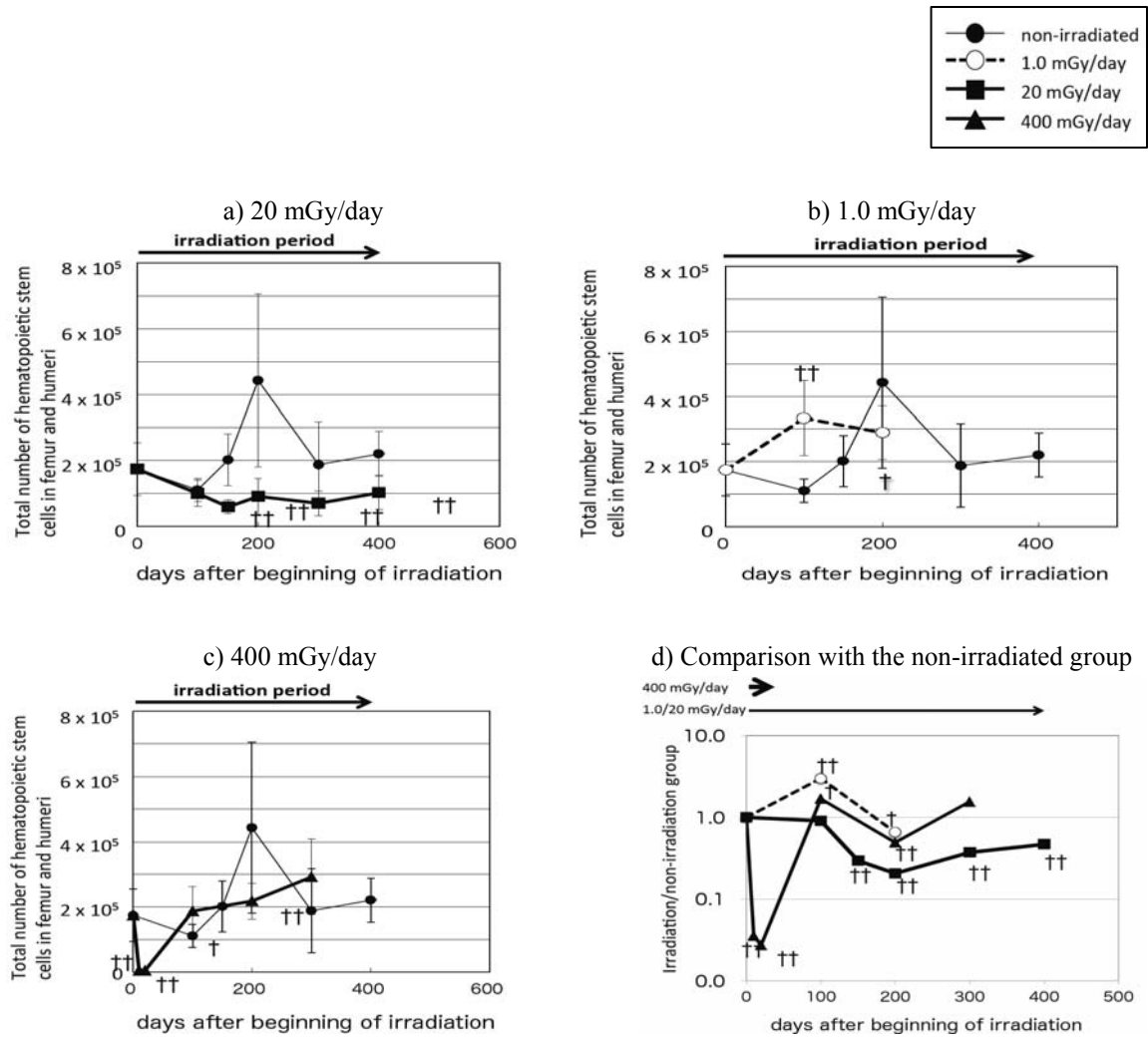


Fig. 1 Change in the number of hematopoietic stem cells over time in mice exposed to γ -rays